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Fax Cover Sheet

Date:	Thursday, April 10, 2008	**Time:**	6:54 PM
To:	Commissioner for Patents United States Patent and Trademark Office	**Phone:** **Fax:**	none 1-571-273-8300
From:	Gary R. Fabian Registration No. 33,875	**Phone/Fax:**	(650) 780-9030
Re:	U.S. Patent Application Serial No. 09/410,462		(Onyx Ref. ONYX1046.ORD)

Number Of Pages Including Cover Sheet: 5 (Five pages)

Message

THE ATTACHED DOCUMENTS ARE TO BE MADE OF OFFICIAL RECORD

Transmitted herewith for filing in the above-referenced application are the following documents:

1. Transmittal;
2. Brief on Appeal substitute pages 7-8 (Summary of the Claimed Subject Matter); and
3. Certificates of Transmission by Facsimile.

Onyx Dkt No. 1046.ORD
USSN: 09/410,462
PATENT

CERTIFICATE OF TRANSMISSION BY FACSIMILE (37 CFR 1.8)		
I hereby certify that this correspondence is being facsimile transmitted to the Commissioner for Patents, United States Patent and Trademark Office, (Fax No. 571-273-8300) on the date indicated.		
Gary R. Fabian	Gary R. Fabian	10 April 2008
Printed Name	Signature	Date of Transmittal

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE	
In Re Application of: Williams, A., et al.	Confirmation No. 6889
Serial No.: 09/410,462	Art Unit: 1635
Filing Date: 1 October 1999	Examiner: J.E. Angell
Title: A SINGLE AGENT METHOD FOR KILLING TUMOR AND TUMOR ASSOCIATED ENDOTHELIAL CELLS USING ADENOVIRAL MUTANTS	

TRANSMITTAL

Mail Stop: Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

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Response to Notification of Non-Compliant Appeal Brief.

A Notification of Non-Compliant Appeal Brief, dated 10 March 2008, was received by appellants. The period for response was set to One Month or Thirty Days, whichever is longer. This response is being forwarded on 10 April 2008, that is, within the One Month period of response.

In the Notification, the Patent Appeal Center Specialist stated the following:

Item 4. Only the claims involved in the appeal should be included in this section of

the Appeal Brief. Please note, the entire Appeal Brief does not need to be resubmitted.

In response to the Notification, appellants have removed the description of claims not subject to appeal from pages 7-8 of the Appeal Brief. Pages 7-8 correspond to the section titled "Summary of the Claimed Subject Matter." Only substitute pages 7-8 accompany this response. The page numbering of the Appeal Brief has not been changed by this substitution.

Appellants believe that accompanying pages 7-8 overcome the objection to the Appeal Brief. Appellants respectfully request entry of the substitute pages and acceptance of the Appeal Brief.

If the Specialist notes any further matters that the Specialist believes may be expedited by a telephone interview, the Specialist is requested to contact Gregory Giotta at (510) 597-6502 or the undersigned at (650) 780-9030.

Authorization to Charge Deposit Account.

No additional fee is believed due; however, the Commissioner is hereby authorized to charge to Deposit Account No. 15-0615 any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, with the exception of the payment of the issue fee.

Respectfully submitted,

Dated: 10 April 2008

By: Gary R. Fabian

Gary R. Fabian, Ph.D.
Registration No. 33,875
Agent for Appellants

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SUMMARY OF THE CLAIMED SUBJECT MATTER

There are three groups of claims pending in the present application. The first group of claims contains independent claims 26-28, which are allowed and not under appeal. The second group of claims relates to independent claim 11 and its dependent claims. The third group of claims relates to independent claim 15 and its dependent claims.

Claims 11, 6, 7 and 15, 17, and 18 of the second and third groups, respectively, are under appeal and generally relate to methods of killing dividing endothelial cells (*e.g.*, microvascular endothelial cells) with substantially less killing of quiescent endothelial cells using a replication competent adenovirus comprising a mutation in an E1A CR2 RB family member binding region.

In the second group of claims, the claims are directed to a method for killing dividing endothelial cells with substantially less killing of the quiescent endothelial cells (independent claim 11; *see, e.g.*, specification, Abstract; page 9, line 22, to page 10, line 2; page 12, lines 10-15; original claim 11). The method comprising contacting a cell population, comprising dividing and quiescent endothelial cells, under infective conditions with a replication competent adenovirus (*see, e.g.*, specification, page 9, line 22, to page 10, line 2; page 6, lines 11-19; original claim 11). The adenovirus comprises a mutation in an E1A CR2 RB family member binding region of the adenovirus (*see, e.g.*, specification FIG. 1; page 4, lines 4-6; original claim 11). A sufficient time for the mutant adenovirus to infect the cell population is allowed (*see, e.g.*, specification page 9, line 9, to page 10, line 2; original claim 11). The mutant adenovirus replicates to higher titers in the dividing cells than wild type adenovirus (*see, e.g.*, specification Abstract; Example 2, pages 17-18; original claim 11). The contacting is by direct administration of the replication competent adenovirus to the cell population (*see, e.g.*, specification pages 13-14; and Examples 3 and 4, pages 18-20).

The mutation in the E1A-CR2 region may, in an adenovirus type 5, comprise a deletion or substitution of one or more amino acids 122 through 129 encoded by the E1A-CR2 region (*see* pending claim 6). Alternatively, the mutation in the E1A-CR2 region may, in an adenovirus type 5, comprise a deletion or substitution of one or more amino acids 111 through 123 (*see* pending claim 7). Dependent claims 8, 9, and 10 are objected to and are not under appeal.

In the third group of claims, the claims are directed to a method for controlling angiogenesis in an animal by substantially and selectively killing dividing microvascular endothelial cells compared to quiescent microvascular endothelial cells (independent claim 15; *see, e.g.*, specification Abstract; page 3, lines 8-11; page 6, lines 27-30; page 9, line 22, to page 10, line 2; page 12, lines 10-32; original claim 15). The method comprises administering to the animal in need of the control a replication competent adenovirus comprising a mutation in an E1A-CR2 RB family member binding region of the adenovirus (*see, e.g.*, specification FIG. 1; page 4, lines 4-6; page 9, line 22, to page 10, line 2; page 6, lines 11-19; original claim 15). A sufficient time for the mutant adenovirus to infect the microvascular endothelial cells is allowed (*see, e.g.*, specification page 9, line 9, to page 10, line 2; original claim 15). The administering is by direct administration of the replication competent adenovirus to the microvascular endothelial cells (*see, e.g.*, specification pages 13-14; and Examples 3 and 4, pages 18-20).

The mutation in the E1A-CR2 region may, in an adenovirus type 5, comprise a deletion or substitution of one or more amino acids 122 through 129 encoded by the E1A-CR2 region (*see* pending claim 17). Alternatively, the mutation in the E1A-CR2 region may, in an adenovirus type 5, comprise a deletion or substitution of one or more amino acids 111 through 123 (*see* pending claim 18). Dependent claims 19, 20, and 34 are objected to and are not under appeal.

The rejection of independent claims 11 and 15, as well as dependent claims 6, 7, 17 and 18 are the subject of this appeal.